Can MELD score be a predictor of liver metastasis in colorectal cancer?

MELD in colorectal cancer

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Abstract

Aim: A significant number of patients with colorectal cancer (CRC) present with liver metastasis at initial diagnosis. The Model for End-Stage Liver Disease (MELD) score consists of three parameters including bilirubin, creatinine and International Normalized Ratio (INR), and is primarily used to rank the priority of patients awaiting liver transplantation. The aim of the study is to investigate the predictive value of MELD score for liver metastasis in patients with CRC. Material and Method: A total of 436 patients diagnosed as CRC were included in the study. The patients were divided into two groups: patients without liver metastasis and those with liver metastasis. The association between MELD score and presence of liver metastasis was investigated. Results: There were 256 (57.9%) males and 183 (41.1%) females, with an overall mean age of 64 years. Liver metastasis was found in 58 (13.2%) patients. Mean MELD score was found to be 8.88 in patients with hepatic metastasis whereas the patients without metastatic liver disease had a mean MELD score of 8.61 (p=0.015). Discussion: MELD score is significantly higher in patients with liver metastasis than in those without liver metastasis. Further studies may help to confirm this result and to determine a possible cut-off value of MELD score.

Keywords

Colorectal Cancer; Liver Metastasis; The Model for End; Stage Liver Disease (MELD) Score

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Introduction

Colorectal cancer (CRC) is the third most common cancer in men and second in women worldwide [1]. Treatment options mainly include surgery and radiochemotherapy, and differ depending on the stage of tumor at the initial diagnosis. Today, various imaging modalities such as ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET/CT) are widely used in the preoperative staging. Stage IV is defined as distant metastasis in one or more organ/site or the peritoneum. Among all metastasis sites, liver is the most frequently affected organ, probably due to the tumoral spread through the portal system [2, 3]. Approximately 20-25% of patients with CRC have synchronous hepatic metastasis at the time of diagnosis, and only a minority of those are suitable for surgery [4-6]. Therefore, detecting liver metastasis is of great importance for the management of such patients. Despite the high specificity and sensitivity rates, there are several drawbacks related to current imaging modalities, including insufficiency in detecting small lesions, technical difficulties, access problems, and high costs.

The Model for End-Stage Liver Disease (MELD) score has been widely used to rank the priority of patients awaiting liver transplantation [7]. This scoring system was also used to predict survival in patients undergoing transjugular intrahepatic portosystemic shunts and those with gastrointestinal bleeding due to portal hypertension [8, 9]. MELD score, based on three parameters including serum creatinine, serum bilirubin, and International Normalized Ratio (INR), is a strong indicator for the status of liver functions. Hepatic dysfunction can be also seen in metastatic liver disease, similar to other causes of hepatic failure. Therefore, in this study, we aimed to investigate whether MELD score may be used as an indicator of liver metastasis in patients with CRC.

Material and Method

Patients and study design

The medical records of 436 patients who were diagnosed as colorectal adenocarcinoma between 2010 and 2016 at Ankara Numune Training and Research Hospital were reviewed retrospectively. The study was conducted according to the Helsinki Declaration. Informed consent of the patients was waived due to the retrospective nature of the study. Patients' demographics including age and gender, preoperative serum levels of creatinine, bilirubin, and INR, MELD score, tumor localization, presence of liver metastasis (according to US, CT, and/or intraoperative findings), and type of initial treatment (surgery or medical) were recorded in detail.

Exclusion criteria were missing medical records, having any hematologic disease causing abnormality in coagulation parameters, having chronic renal insufficiency, use of drugs which led disturbance in coagulation tests, and having another type of cancer.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS 21.0 IL-Chicago- USA) standard version was used for data analyses. Descriptive analysis was done for demographic, laboratory and operative variables. The results were presented as mean ± SD/ percentages for continuous variables and number/percentage for categorical variables. Kolmogorov-Smirnov test was used to test the normality of variables between patients with liver metastasis and those without liver metastasis. Chi-square (x2) test, Fisher's Exact test and Mann Whitney U test were used to test for the significance of association between the two patient groups. Significance level was accepted as $p < 0.05$.

Results

A total of 439 patients (mean age 64 years) who met the study criteria were included in the study. There were 256 (57.9%) males and 183 (41.1%) females. US and CT were performed in all patients during the preoperative period. Rectum (43.9%) was the most common localization, and low anterior resection (34.2%) was the most performed surgical operation. All demographic data, laboratory tests, and perioperative findings of patients are presented in Table 1.

Table 1. The baseline characteristics of the patients (n=439)

Patient characteristics	n (%)
Age (year)	64.04±13.1 (26-95)
Gender	
Male	257 (58.5%)
Female	182 (41.5%)
Creatinine (mg/dL)	1.17±0.6 (1-9.05)
Bilirubin (mg/dL)	1.05±0.2 (1-3.6)
INR	1.12±0.4 (1-10.5)
MELD score	8.64±3.4 (6.43-33.62)
Localization of tumor	
Rectum	193 (43.9%)
Right colon	119 (27.1%)
Left colon	116 (26.4%)
Right+left colon	11 (2.5%)
Type of treatment	
Anterior/low anterior resection	151 (34.4%)
Right hemicolectomy	110 (25%)
Left hemicolectomy	53 (12.1%)
Sigmoidectomy	31 (7.1%)
Subtotal/total colectomy	10 (2.3)
Hepatic resection	32 (7.3%)
Others*	14 (3.2%)
Non-surgical**	70 (15.9%)

Age, creatinine, bilirubin, and INR were presented as mean±SD; other variables were presented as number (%). *Others: colostomy, by-pass operation, and exploration only. **Non-surgical: Patients who were subjected to neoadjuvant/adjuvant therapy or refused surgery

All patients were divided into two groups: patients without liver metastasis (group 1) (381, 86.8%) and those with liver metastasis (group 2) (58, 13.2%). Among patients in group 2, metastatic hepatic lesions were radiologically detected in 56. On the other hand, in two patients who had no signs of hepatic metastasis on US and/ CT, liver metastases were found intraoperatively. Mean MELD score was found to be 8.88 in group 2 whereas the patients in group 1 had a mean MELD score of 8.61 (p=0.015).

Patients with liver metastasis were significantly younger than those without liver metastasis (p=0.006). There were no significant differences in other parameters between the two groups (p>0.05). The comparison of demographic, laboratory, and operative findings between the two patient groups are given in Table 2.

Table 2. The comparison of demographic data, operative findings, and MELD score between the two groups

Parameters	Group 1 (n=381)	Group 2 (n=58)	p
Age (mean)	64.6±13.3 (26-95)	59.6±11.07 (31-84)	0.006
Gender (M/F)	216/164	35/23	0.165
MELD score	8.61±3.4 (6.43-33.6)	8.88±2.9 (6.4-19.9)	0.015
Localization of tumor			0.822
Rectum	169 (44.3%)	24 (41.4%)	
Right colon	102 (26.8%)	17 (29.3%)	
Left colon	102 (26.8%)	14 (24.1%)	
Right+left colon	8 (2.1%)	3 (5.2%)	
Type of treatment			0.519
Anterior/low anterior resection	132 (34.6%)	19 (32.7%)	
Right hemicolectomy	96 (25.2%)	14 (24.1%)	
Left hemicolectomy	47 (12.3%)	6 (10.3%)	
Sigmoidectomy	27 (7.1%)	4 (6.9%)	
Subtotal/total colectomy	8 (2.1%)	2 (3.4%)	
Hepatic resection	23 (6%)	9 (15.5%)	
Others*	12 (3.2%)	2 (3.4%)	
Non-surgical**	59 (15.5%)	11 (18.9%)	

M: Male, F: Female, *Others: colostomy, by-pass operation, and exploration only. **Non-surgical: Patients who were subjected to neoadjuvant/adjuvant therapy or refused surgery

Discussion

Liver is the most common metastasis site in CRC, and its management differs from other metastatic sites. The number, size, and proximity of hepatic tumors to key vascular and biliary structures, and the status of hepatic reserve are taken into consideration for surgical planning. For this reason, various imaging studies are widely used for the identification of patients for surgical and non-surgical therapies. US is an inexpensive and easily available imaging test, and is usually considered as the first line imaging method for determining liver metastasis in patients with CRC. However, it has some limitations such as operator dependence, ambiguity in segmental localization, which is crucial for surgical planning, and poor performance in the presence of hepatic steatosis and diffuse and chronic hepatic disease [7]. Thus, US has largely been supplanted by CT and MR. CT is the most commonly used imaging test in the preoperative evaluation of patients with CRC, and advantages include improved detection of small lesions and accurate segmental localization of metastatic lesions. However, difficulties in detection of liver metastasis in the presence of fatty liver and low sensitivity rates in identifying lesions less than 1 cm are the main handicaps of this imaging modality [8, 9]. MR is superior to US and CT in evaluation of hepatic metastasis by providing heightened soft-tissue resolution [10]. On the other hand, small hemangiomas are often difficult to differentiate from metastases by MR imaging [11]. PET/CT is a new but expensive imaging method. The role of this diagnostic modality is stil not well-defined, and is recommended only for the evaluation of recurrent lesions and in preoperative staging prior to metastasectomy [11]. As seen, none of these imaging modalities is fully capable of identifying liver metastases in CRC. Because of this, a combination of these modalities is usually used for preoperative evaluation of patients, leading to increased health costs and loss of time.

In this contex, we hypothesized that MELD score, which is primarily used for the classification of patients awaiting liver transplantation, may be an indicator of liver metastasis in patients with CRC. The main reason for considering this is the components of the MELD score. As is well known, the MELD score consists of three biochemical parameters, serum creatinine, serum total bilirubin, and INR, regardless of the etiology of the liver disease. Of these three variables, serum bilirubin carries the most weight. It is a well-known marker of both hepatic synthetic function and excretory function [12]. Another parameter of MELD score is INR, which reflects coagulopathy associated with synthetic dysfunction of the liver [13]. Coagulation disorders due to various causes such as decreased synthesis of clotting and inhibitor factors, decreased clearance of activated factors, platelet defects, hyperfibrinolysis, and accelerated intravascular coagulation are common in chronic liver diseses [14]. Serum creatinine is the third componenet of MELD score, and allows a noninvasive measurement of renal function.

MELD is not only used to stratify patients with end-stage liver disease for liver transplantation, but there are also several clinical applications for MELD use, such as prediction of mortality in patients with acute variceal bleeding and trauma patients, determination of surgical risk in patients with cirrhosis, and estimation of clinical outcomes in patients with hepatorenal syndrome [15-18]. Similarly, hepatic dysfunction can develop in patients with metastatic liver disease, depending on the extent and localization of the lesions. For instance, hyperbilirubinemia caused by various factors such as metastatic portal lymph node enlargement and replacement of hepatic parenchyma by cancerous tissue is not a rare condition in these patients, and is associated with poor prognosis [19]. In addition, coagulation disorders can develop in cancer patients with or without liver metastasis. Many different types of coagulopathy can be seen in these patients, and are related to various causes including tumor-specific growth characteristics, neoangiogenesis, defective myelopoiesis, hypoproteinemia, and metastatic lesions growth with organ dysfunction [20]. Thus, the association between pathological changes in these laboratory parameters and metastatic liver disease suggests that this scoring system may be used as an indicator of the presence of hepatic metastasis in patients with CRC. The results obtained from the present study also supported this hypothesis. To the best of our knowledge, there is no study on this topic in the literature, and our study is the first indicating the high predictive value of MELD score for liver metastasis in patients with CRC.

Conclusion

According to the results obtained from the present study, MELD score is significantly higher in patients with liver metastasis than in those without liver metastasis, indicating the high predictive value of MELD score for liver metastasis. This is important because provides a new application field for the MELD score, in addition to its routine use. However, further studies are needed to confirm the results and to determine a possible cut-off value of MELD score in predicting hepatic metastasis.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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